

# Setting Individualized Positive End-Expiratory Pressure Level with a Positive End-Expiratory Pressure Decrement Trial After a Recruitment Maneuver Improves Oxygenation and Lung Mechanics During One-Lung Ventilation

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**BACKGROUND:** We investigated whether individualized positive end-expiratory pressure (PEEP) improves oxygenation, ventilation, and lung mechanics during one-lung ventilation compared with standardized PEEP.

**METHODS:** Thirty patients undergoing thoracic surgery were randomly allocated to the study or control group. Both groups received an alveolar recruitment maneuver at the beginning and end of one-lung ventilation. After the alveolar recruitment maneuver, the control group had their lungs ventilated with a 5 cm-H<sub>2</sub>O PEEP while the study group had their lungs ventilated with an individualized PEEP level determined by a PEEP decrement trial. Arterial blood samples, lung mechanics, and volumetric capnography were recorded at multiple timepoints throughout the procedure.

**RESULTS:** The individualized PEEP values in study group were higher than the standardized PEEP values ( $10 \pm 2$  vs 5 cm-H<sub>2</sub>O;  $P < 0.001$ ). In both groups, arterial oxygenation decreased when bilateral-lung ventilation was switched to one-lung ventilation and increased after the alveolar recruitment maneuver. During one-lung ventilation, oxygenation was maintained in the study group but decreased in the control group. After one-lung ventilation, arterial oxygenation was significantly higher in the study group (306 vs 231 mm-Hg,  $P = 0.007$ ). Static compliance decreased in both groups when bilateral-lung ventilation was switched to one-lung ventilation. Static compliance increased significantly only in the study group ( $P < 0.001$ ) after the alveolar recruitment maneuver and optimal PEEP adjustment. The alveolar recruitment maneuver did not decrease cardiac index in any patient.

**CONCLUSIONS:** During one-lung ventilation, the improvements in oxygenation and lung mechanics after an alveolar recruitment maneuver were better preserved by ventilation by using individualized PEEP with a PEEP decrement trial than with a standardized 5 cm-H<sub>2</sub>O of PEEP. (Anesth Analg 2014;118:657–65)

In many surgical procedures, one-lung ventilation is required to provide optimum surgical exposure. During one-lung ventilation, a shunt-like effect may arise from continued perfusion of the nonventilated lung and inadequate expansion of the ventilated-dependent lung in the presence of a high inspired O<sub>2</sub> fraction (F<sub>IO<sub>2</sub></sub> = 1.0) or related to anesthesia and position.<sup>1</sup> Lung-protective ventilation strategies can reduce acute lung injury<sup>2–6</sup> but may promote alveolar collapse as a consequence of low tidal volume.<sup>7,8</sup> Atelectasis prevention during lung-protective ventilation requires positive

end-expiratory pressure (PEEP)<sup>9–11</sup>; however, optimal PEEP levels and actual effects of PEEP are not clear.<sup>12–19</sup>

Two reviews suggest that application of 5 cm-H<sub>2</sub>O PEEP after an alveolar recruitment maneuver is the best method for treating ventilation-perfusion mismatch during one-lung ventilation.<sup>20,21</sup> Several clinical studies of thoracic surgery with one-lung ventilation have reported improved oxygenation and ventilation when an alveolar recruitment maneuver is performed with a standardized PEEP of 5 to 10 cm-H<sub>2</sub>O.<sup>22–26</sup> However, individualized PEEP determined by using a PEEP decrement titration trial after an alveolar recruitment maneuver also improves oxygenation, ventilation, and lung mechanics in anesthetized patients with healthy lungs or lung injury.<sup>27–29</sup>

There are no reported studies of the effects of an alveolar recruitment maneuver with individualized PEEP settings titrated with a PEEP decrement trial during one-lung ventilation in thoracic surgery. We hypothesized that such a procedure would improve gas exchange and lung mechanics compared with the establishment of a standardized 5 cm-H<sub>2</sub>O PEEP after an alveolar recruitment maneuver during one-lung ventilation. We performed a prospective, randomized controlled trial to test this hypothesis.

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## METHODS

The study was performed at the Department of Anesthesiology and Critical Care at the Hospital Clínico Universitario de Valencia, Spain, from May to December 2012. Written informed consent was obtained from all patients, and the study was approved by the Local Ethics Committee for Clinical Research. The study included patients with ASA physical status I to III undergoing elective lung resection. Exclusion criteria were age <18 years, ASA physical status IV, pneumonectomy, New York Heart Association III to IV, and preoperative hemoglobin <10 mg/dL.

## General Procedures

Patients were monitored for nasopharyngeal temperature, electrocardiogram, pulse oximetry, and invasive arterial blood pressure by using the GE Aisys Carestation™ monitor. The depth of anesthesia was monitored with the Bispectral Index (BIS vista, Aspect Medical Systems, The Netherlands) and cardiac index with the Vigileo (Edwards Lifesciences, Irvine, CA). Despite cardiac output measurement by using pulse contour analysis not being validated during one-lung ventilation, this method has been used in previous studies with consistent results.<sup>30,31</sup>

Before anesthesia induction, a thoracic epidural catheter (Tuhoy; Braun Laboratories, Melsungen AG, Germany) was placed at T3 to T6, and 3 mL bupivacaine 0.25% with epinephrine was administered. After 5 minutes breathing 100% oxygen, anesthesia was induced with fentanyl 5  $\mu\text{g}\cdot\text{kg}^{-1}$ , propofol 2.5  $\text{mg}\cdot\text{kg}^{-1}$ , and rocuronium 0.6  $\text{mg}\cdot\text{kg}^{-1}$ . Sevoflurane was administered to maintain a BIS between 40 and 50. Patients received a continuous infusion of remifentanyl 0.1 to 0.4  $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ . Crystalloid solutions were continuously infused at a rate of 3  $\text{mL}\cdot\text{kg}^{-1}\cdot\text{h}^{-1}$ . The trachea was intubated with an appropriately sized left-side double-lumen tube (Broncho-part; Rush, Kernen, Germany). Tube position was confirmed by bronchoscopy in the supine and lateral positions.

The patient's lungs were ventilated with the GE Aisys Carestation™ by using volume-controlled ventilation with square-wave flow. Tidal volume was set to 8  $\text{mL}\cdot\text{kg}^{-1}$  of predicted body weight during 2-lung (bilateral) ventilation and 5 to 7  $\text{mL}\cdot\text{kg}^{-1}$  during one-lung ventilation to maintain a plateau pressure  $\leq 25\text{ cm}\cdot\text{H}_2\text{O}$ . When plateau pressure was above 25  $\text{cm}\cdot\text{H}_2\text{O}$ , tidal volume was reduced in 1  $\text{mL}\cdot\text{kg}^{-1}$  steps until plateau pressure  $\leq 25$ . To avoid hypoxemia during one-lung ventilation and interference from  $\text{FIO}_2$  in the measurement of  $\text{PaO}_2$ , we used 100%  $\text{FIO}_2$  during the study period. The inspiratory-to-expiratory ratio was 1:2 with an end-inspiratory pause of 10%, and frequency was adjusted to maintain arterial  $\text{CO}_2$  partial pressure ( $\text{Paco}_2$ ) between 35 and 60 mm-Hg. All patients had an initial PEEP level of 5  $\text{cm}\cdot\text{H}_2\text{O}$  during bilateral-lung ventilation, which was maintained in the control group throughout the study.

## Monitoring

Intraoperative blood gas was monitored with the i-STAT® Analyzer (Abbott laboratories, East Windsor, NJ), which measured acid-base status (pH), oxygen arterial pressure ( $\text{PaO}_2$ ), and  $\text{Paco}_2$ .

Static compliance during volume-controlled ventilation and dynamic compliance during pressure-controlled

ventilation, airway resistance, peak inspiratory pressure, and plateau pressure were determined by using the NICO capnograph (Respironics, Wallingford, CT). Static compliance was calculated as tidal volume/(plateau pressure–total PEEP). Alveolar dead space was measured by using volumetric capnography. We calculated the ratios of physiological and alveolar dead-space to tidal volume (physiologic dead-space volume/tidal volume and alveolar dead-space volume/alveolar tidal volume, respectively), by applying the Bohr-Enghoff formula<sup>32</sup> as previously described.<sup>22–26</sup> The presence of auto-PEEP was evaluated in real-time by observing the flow-volume curves on the Nico monitor.<sup>33</sup> In the presence of an interrupted expiratory flow, inspiratory flow began before expiratory flow ceased, that is, reached zero, suggesting that passive expiration is incomplete, and the airway pressure reflects the recoil pressure of the respiratory system (auto-PEEP) at the elevated end-expiratory volume.

## Experimental Protocol

Measurements during one-lung ventilation were performed with the patients in lateral position, with pleura opened, after collapse of the nondependent lung.

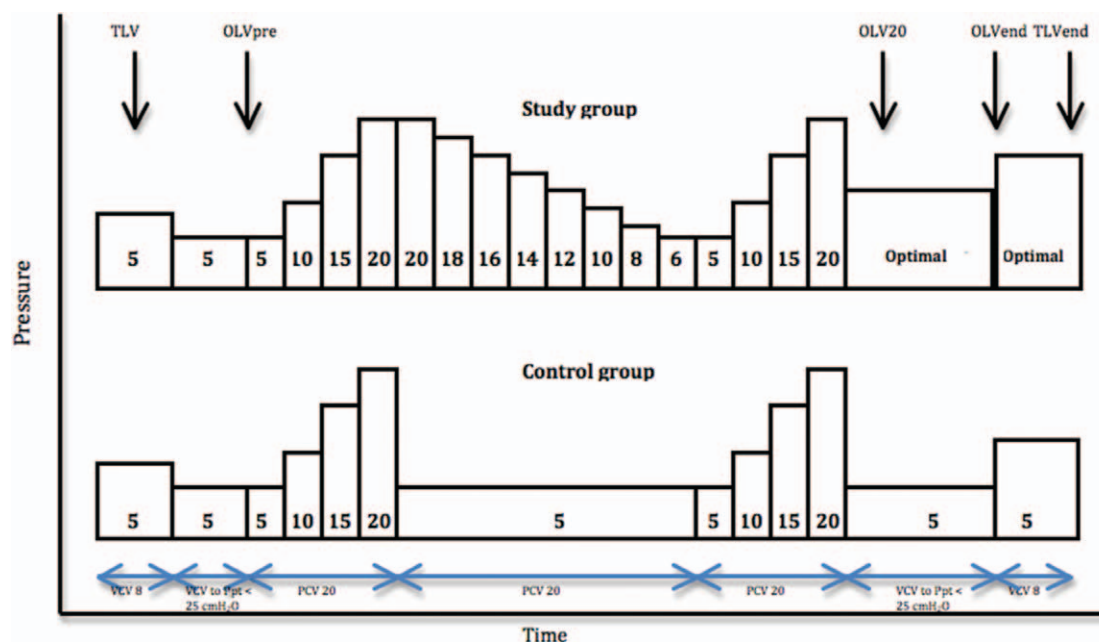
In the study group, one-lung ventilation was initiated after checking the correct position of the double-lumen tube and correct sealing of both cuffs. The recruitment maneuver was applied to the dependent lung following a standard protocol. The ventilator was switched to pressure-control ventilation with a driving pressure of 20  $\text{cm}\cdot\text{H}_2\text{O}$  and 15 bpm. PEEP was increased in 5  $\text{cm}\cdot\text{H}_2\text{O}$  steps and was held at each step for 10 breaths. A recruitment opening pressure of 40  $\text{cm}\cdot\text{H}_2\text{O}$  (20  $\text{cm}\cdot\text{H}_2\text{O}$  of driving pressure and 20  $\text{cm}\cdot\text{H}_2\text{O}$  PEEP) was applied for 20 breaths.<sup>26</sup> After the alveolar recruitment maneuver was performed, a PEEP decrement trial was initiated. PEEP was decreased in 2  $\text{cm}\cdot\text{H}_2\text{O}$  steps until the maximal dynamic compliance was obtained, which was considered the individualized (optimal) PEEP level.<sup>29</sup> The duration of each step was 2 minutes. Thereafter, a new alveolar recruitment maneuver was performed as described above. The ventilator was switched to volume-controlled ventilation, and the individualized PEEP level was established and maintained throughout the study period.

In the control group, the same procedures were followed except for the PEEP titration (Fig. 1). After an alveolar recruitment maneuver, a level of 5  $\text{cm}\cdot\text{H}_2\text{O}$  PEEP was fixed. The second alveolar recruitment maneuver was performed 10 minutes after the first, and a PEEP level of 5  $\text{cm}\cdot\text{H}_2\text{O}$  was again established and maintained during the study period.

After the one-lung ventilation period and before bilateral-lung ventilation, a sustained manual expansion of the reservoir bag (40  $\text{cm}\cdot\text{H}_2\text{O}$  for 10 seconds) of the nondependent lung was performed in all patients, without altering the PEEP level.

All studied variables were recorded at 5 different timepoints:

1. during bilateral-lung ventilation 10 minutes after intubation,
2. during one-lung ventilation 5 minutes after collapse of the nondependent lung (pleura opened) and before the alveolar recruitment maneuver,



**Figure 1.** VCV 8 = volume-control ventilation with tidal volume set to 8 mL·kg<sup>-1</sup>. VCV 6 = volume-control ventilation with tidal volume set to 5 to 7 mL·kg<sup>-1</sup>. PCV = pressure-control ventilation with 20 cm·H<sub>2</sub>O. Optimal = PEEP with best dynamic compliance. Pressure = airway pressure.

3. during one-lung ventilation 20 minutes after applying PEEP (5 cm·H<sub>2</sub>O in the control group and optimal PEEP in the study group),
4. at the end of one-lung ventilation before reexpansion of the nondependent lung,
5. at the end of bilateral-lung ventilation just before extubation.

### Statistical Analysis

Based on previous studies,<sup>23</sup> it was estimated that a total of 30 patients were needed to detect at least a 10% difference in oxygenation at the end of one-lung ventilation, with a 5% significance level and 80% power. The Kolmogorov-Smirnov with Lilliefors correction test was performed for variable normality and Levene's test was used for homogeneity of variances. When the homogeneity hypothesis was rejected (test *P* value <0.05), the Mann-Whitney *U* test and Friedman were applied. This test was used for airway resistance, where the magnitude of heterogeneity of variances between groups is not enough to influence conclusions.<sup>34</sup> If the null hypothesis was not rejected, a Student *t* test and analysis of variance (ANOVA) were performed. For multiple comparisons, the Bonferroni correction was used to maintain the risk of a type 1 error at the chosen significance level ( $\alpha = 0.05$ ). When Bonferroni was used, *P*-values and confidence intervals (CI) are presented as "corrected." The denominator for the correction was the total number of comparisons for each variable (5, corresponding to the 5 times). The parameters are presented as mean ( $\pm$ SD). Statistical analysis was performed by using the SPSS 15.0 software package (SPSS, Chicago, IL).

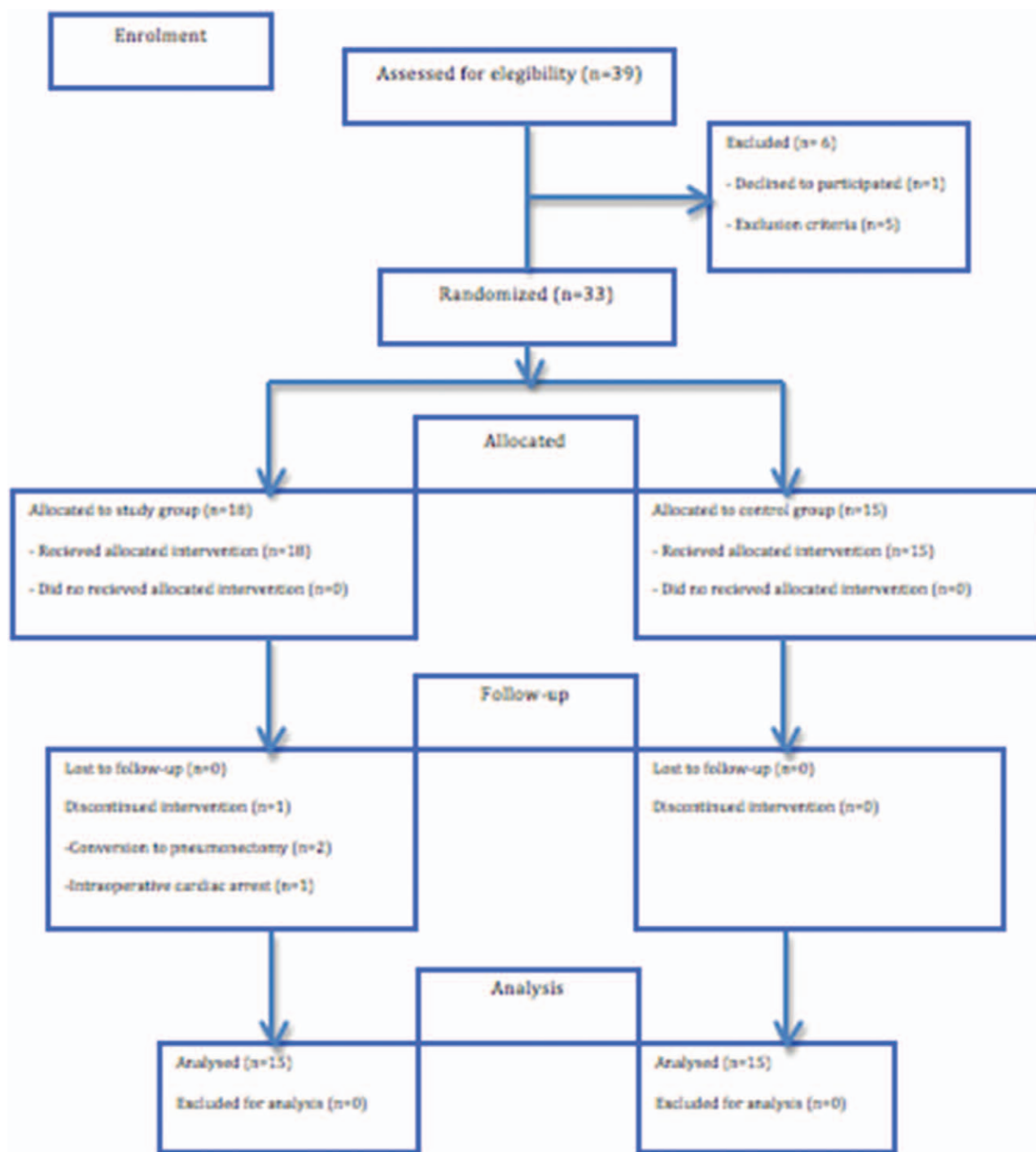
### RESULTS

Thirty patients undergoing thoracic surgery were studied (Fig 2). Table 1 presents the demographic data. There were no baseline differences between the 2 groups. In the study

group, individualized PEEP during the PEEP titration trial was 10 ( $\pm$ 2) cm·H<sub>2</sub>O, which was significantly different from the 5 cm·H<sub>2</sub>O used in the control group (95% CI of the difference was +4 to +6 cm·H<sub>2</sub>O, *P* < 0.001). Fig. 3 shows dynamic compliance versus PEEP in the study group during the PEEP decrement trial.

In both groups, arterial oxygenation decreased by approximately 50% when bilateral-lung ventilation was switched to one-lung ventilation and increased after an alveolar recruitment maneuver (Table 2). Thereafter, oxygenation during one-lung ventilation was maintained in the study group and decreased in the control group by 18% at the end of one-lung ventilation (Table 2). At the end of one-lung ventilation, arterial oxygenation was significantly higher (*P* = 0.007) with the individualized PEEP when compared with 5 cm·H<sub>2</sub>O (Table 3). The sample size was relatively small to evaluate differences in the PaO<sub>2</sub>/Fio<sub>2</sub> between surgical sites (right versus left). In the control group, with bilateral-lung ventilation, the 95% CI of the difference was -108 to +165 mm·Hg, *P* = 0.62, and with one-lung ventilation 20 minutes after PEEP, the 95% CI of the difference was -211 to +25 mm·Hg, *P* = 0.10. In the study group, with bilateral-lung ventilation, the 95% CI of the difference was -176 to +111, *P* = 0.60, and with one-lung ventilation 20 minutes after PEEP, the 95% CI of the difference was -199 to +43, *P* = 0.16. When all patients with bilateral lung ventilation were compared, the 95% CI of the difference was -29 to +115, *P* = 0.22 and with one-lung ventilation 20 minutes after PEEP, the 95% CI of the difference was -150 to +23, *P* = 0.14.

In both groups, static compliance decreased when bilateral-lung ventilation was switched to one-lung ventilation (Table 2). After an alveolar recruitment maneuver, static compliance increased significantly in the study group (corrected 95% CI of the difference was +3 to +30 mL cm·H<sub>2</sub>O<sup>-1</sup>, corrected *P* < 0.007) and remained increased throughout



**Figure 2.** Flow diagram.

one-lung ventilation (Table 2). The results obtained for compliance in the control group after alveolar recruitment were inconclusive (Table 2).

Peak inspiratory pressures showed no differences between groups despite the higher PEEP levels in the study group (Table 4). Airway resistance increased in both groups when bilateral-lung ventilation changed to one-lung ventilation (in the study group, corrected 95% CI of the difference was +3 to +14 cm·H<sub>2</sub>O, corrected  $P < 0.001$  and in the control group, corrected 95% CI of the difference was +2 to

+12 cm·H<sub>2</sub>O, corrected  $P < 0.001$ ), and remained increased throughout one-lung ventilation (Table 4). No differences were found between groups (Table 4). None of the study patients had auto-PEEP during the study period.

After an alveolar recruitment maneuver and PEEP adjustment, tidal volume was reduced in most patients in the study group to keep plateau pressure below 25 cm·H<sub>2</sub>O. In these patients, the ventilatory rate was increased to keep PaCO<sub>2</sub> within the target range. Hence, tidal volume trended slightly lower, and ventilatory rate tended higher



**Table 1. Demographic Data**

	Study group	Control group
No. patients	15	15
Age	61 (9)	67 (9)
PBW (kg)	63 (8)	63 (6)
ASA II/III	3/12	4/11
Preoperative FVC (%predicted)	93 (19)	94 (17)
Preoperative FEV <sub>1</sub> (%predicted)	91 (23)	87 (24)
Preoperative FEV <sub>1</sub> /FVC (%predicted)	76 (9)	79 (17)
Hemoglobin (g/dL)	14.9 (1.4)	14.6 (1.9)
Duration of mechanical ventilation (min)	172 (46)	173 (49)
Duration one-lung ventilation (min)	119 (44)	135 (50)
Surgical site R/L	7/8	8/7

Mean (SD) for continuous variables and *n* for categorical variable.

PBW = predicted body weight; FVC = forced vital capacity; FEV<sub>1</sub> = forced expiratory volume; MV = mechanical ventilation; One-Lung Ventilation = one-lung ventilation; R = right; L = left.

in the control group during one-lung ventilation. Paco<sub>2</sub> was higher in the study group since the initial measurement during bilateral-lung ventilation and the between-group differences did not vary along the study period (Table 3).

Dead-space/tidal volume showed no differences between groups when switching from bilateral-lung ventilation to one-lung ventilation (dead-space volume/tidal volume, *P* = 0.06 and alveolar dead-space volume/alveolar tidal volume, *P* = 0.14). In the study group, alveolar dead-space volume/alveolar tidal volume decreased slightly after an alveolar recruitment maneuver during one-lung ventilation (one-lung ventilation 20 minutes after starting PEEP, corrected 95% CI of the difference was +0.01 to +0.04, corrected *P* < 0.001 and end one-lung ventilation, corrected 95% CI of the difference was +0.007 to +0.04, corrected *P* = 0.002). The results obtained in the control group for alveolar dead-space volume/alveolar tidal volume were inconclusive (Table 2).

The cardiac index did not differ between groups, and the alveolar recruitment maneuver did not produce a cardiac index decrease in any patient (Table 3).

## DISCUSSION

The results of this clinical study show that oxygenation and lung mechanics improvement secondary to the alveolar recruitment maneuver were better maintained during one-lung ventilation with an individualized PEEP level determined with a PEEP decrement trial than with a standardized PEEP level.

We found that an alveolar recruitment maneuver improved oxygenation during one-lung ventilation in both groups. The improvement in oxygenation should be related to a decrease in intrapulmonary shunt as shown by several studies.<sup>26</sup> However, our results showed that only the study group maintained this oxygenation improvement throughout the procedure until the end of one-lung ventilation; the study group also maintained improved static compliance after an alveolar recruitment maneuver, suggesting a constant end-expiratory lung volume. In contrast, in the control group, the improvements in oxygenation and static compliance were not maintained after an alveolar recruitment maneuver, possibly due to a partial loss in the end-expiratory lung volume. These findings suggest that an optimal PEEP level kept the lung

**Table 2. Intragroup Differences of Oxygenation and Ventilatory Variables**

	One-lung ventilation prerecruitment–bilateral lung ventilation	One-lung ventilation 20 min after PEEP–one-lung ventilation prerecruitment	End one-lung ventilation–one-lung ventilation 20 min after PEEP	End one-lung ventilation–one-lung ventilation prerecruitment
Study				
Pao <sub>2</sub> (mm-Hg)	–199; [–293 to –114]*; <i>P</i> < 0.001	61; [26 to 148]*; <i>P</i> = 0.03	5; [–82 to 92]; <i>P</i> = 1.00	65; [22 to 153]*; <i>P</i> = 0.03
Control	–203; [–286 to –111]*; <i>P</i> < 0.001	49; [24 to 134]*; <i>P</i> = 0.04	–51; [–113 to 65]; <i>P</i> = 1.00	2; [–67 to 110]; <i>P</i> = 1.00
Study				
Static compliance (mL·cm-H <sub>2</sub> O)	–16; [–2 to –29]*; <i>P</i> = 0.01	16; [3 to 30]*; <i>P</i> = 0.007	2; [–15 to 12]; <i>P</i> = 1.00	14; [0.2 to 1.1]*; <i>P</i> = 0.02
Control	–19; [–3 to 36]; <i>P</i> = 0.08	3; [–13 to 18]; <i>P</i> = 1.00	–2; [–18 to 13]; <i>P</i> = 1.00	0.2; [–16 to 16]; <i>P</i> = 1.00
Study				
Airway resistance (cm-H <sub>2</sub> O L <sup>–1</sup> s <sup>–1</sup> )	9; [3 to 14]*; <i>P</i> < 0.001	–0.4; [–5 to 5]; <i>P</i> = 1.00	–0.5; [–7 to 6]; <i>P</i> = 1.00	–1; [–7 to 5]; <i>P</i> = 1.00
Control	7; [2 to 12]*; <i>P</i> < 0.001	2; [–2 to 7]; <i>P</i> = 1.00	–0.3; [–6 to 5]; <i>P</i> = 1.00	2; [–3 to 7]; <i>P</i> = 1.00
Study				
Physiologic dead space/tidal volume	0.01; [–0.04 to 0.07]; <i>P</i> = 1.00	–0.03; [–0.09 to 0.02]; <i>P</i> = 0.73	0.009; [–0.04 to 0.06]; <i>P</i> = 1.00	–0.02; [–0.08 to 0.03]; <i>P</i> = 1.00
Control	0.02; [–0.05 to 0.11]; <i>P</i> = 1.00	–0.02; [–0.11 to 0.05]; <i>P</i> = 1.00	0.02; [–0.60 to +0.10]; <i>P</i> = 1.00	–0.002; [–0.08 to 0.08]; <i>P</i> = 1.00
Study				
Alveolar dead space/alveolar tidal volumen	0.008; [–0.10 to 0.02]; <i>P</i> = 1.00	–0.03; [–0.01 to –0.04]*; <i>P</i> < 0.001	0.006; [–0.01 to 0.02]; <i>P</i> = 1.00	–0.02; [–0.04 to –0.007]*; <i>P</i> = 0.002
Control	0.000; [–0.03 to 0.03]; <i>P</i> = 1.00	–0.006; [–0.04 to 0.03]; <i>P</i> = 1.00	0.01; [–0.02 to 0.05]; <i>P</i> = 1.00	0.009; [–0.02 to 0.05]; <i>P</i> = 1.00

Data described as mean of the difference; corrected 95% of the confidence interval and corrected *P* value of the difference.

PEEP = positive end-expiratory pressure.

\**P* < 0.05

**Table 3. Blood Gas and Cardiac Index**

	Bilateral-lung ventilation	One-lung ventilation, prerecruitment maneuver	One-lung ventilation 20 after PEEP	End one-lung ventilation	End bilateral-lung ventilation
pH					
Control	7.36 (0.4) <sup>a</sup>	7.38 (0.5)	7.37 (0.4)	7.35 (0.4)	7.35 (0.6)
Study	7.32 (0.3)	7.34 (0.4)	7.34 (0.5)	7.32 (0.5)	7.31 (0.6)
P-value	0.02	0.06	0.1	0.06	0.12
Pao <sub>2</sub> (mm·Hg)					
Control	436 (84)	229 (87) <sup>b</sup>	280 (67) <sup>c</sup>	231 (85) <sup>a</sup>	438 (139)
Study	439 (88)	240 (102) <sup>b</sup>	301 (79) <sup>c</sup>	306 (73) <sup>c</sup>	501 (99)
P-value	0.92	0.46	0.08	0.007	0.17
Paco <sub>2</sub> (mm·Hg)					
Control	42 (4) <sup>a</sup>	42 (4) <sup>a</sup>	42 (6) <sup>a</sup>	40 (5) <sup>a</sup>	43 (7) <sup>a</sup>
Study	48 (6)	46 (7)	48 (5)	49 (6)	52 (8)
P-value	0.005	0.04	0.006	0.001	0.01
CI (l min <sup>-1</sup> ·m <sup>-2</sup> -1)					
Control	2.6 (0.7)	2.5 (0.5)	2.7 (0.6)	2.5 (0.3)	2.6 (0.6)
Study	2.8 (0.7)	2.7 (0.4)	2.8 (0.5)	2.7 (0.5)	3.0 (0.6)
P-value	0.38	0.06	0.46	0.34	0.07

Data are presented as mean (SD).  $P < 0.05$  in all groups.

PEEP = positive end-expiratory pressure.

<sup>a</sup>Control versus study.

<sup>b</sup>Bilateral versus one-lung ventilation prerecruitment maneuver.

<sup>c</sup>One-lung ventilation prerecruitment maneuver vs 20 minutes after PEEP during one-lung ventilation, and end of one-lung ventilation,  $P$  value for control versus study difference.

**Table 4. Ventilatory Variables**

	Bilateral-lung ventilation	One-lung ventilation, prerecruitment maneuver	One-lung ventilation 20 min after PEEP	End one-lung ventilation	End bilateral-lung ventilation
Static compliance (mL·cm·H <sub>2</sub> O <sup>-1</sup> )					
Control	53 (21)	33 (7) <sup>b</sup>	35 (7) <sup>a</sup>	33 (6) <sup>a</sup>	49 (24)
Study	49 (13)	33 (8) <sup>b</sup>	50 (11) <sup>c</sup>	48 (10) <sup>c</sup>	56 (19)
P-value	0.60	0.96	<0.001	<0.001	0.39
Physiologic dead-space volume/tidal volume					
Control	0.63 (0.4)	0.65 (0.8)	0.62 (0.8)	0.65 (0.8)	0.65 (0.9)
Study	0.65 (0.4)	0.69 (0.5)	0.64 (0.5)	0.64 (0.5)	0.66 (0.5)
P-value	0.10	0.06	0.10	0.27	0.55
Alveolar dead-space volume/alveolar tidal volume					
Control	0.31 (0.2)	0.32 (0.5)	0.31 (0.4)	0.33 (0.4)	0.33 (0.4)
Study	0.32 (0.2)	0.34 (0.2)	0.31 (0.1) <sup>c</sup>	0.31 (0.1) <sup>c</sup>	0.32 (0.1)
P-value	0.11	0.14	0.81	0.56	0.79
Peak inspiratory pressure (cm·H <sub>2</sub> O)					
Control	21 (4)	26 (4) <sup>b</sup>	26 (6)	26 (6)	24 (6)
Study	19 (4)	26 (5) <sup>b</sup>	27 (6)	27 (6)	26 (9)
P-value	0.16	0.67	0.31	0.41	0.53
Tidal volume (mL)					
Control	8 (0)	6.7 (0.4) <sup>b</sup>	6.8 (0.4)	6.8 (0.4)	7.8 (0.4)
Study	8 (0)	6.7 (0.5) <sup>b</sup>	6.4 (0.8)	6.4 (0.8)	7.6 (0.7)
P-value		0.72	0.09	0.05	0.34
Ventilatory rate (breaths/min)					
Control	13(1)	15(1) <sup>b</sup>	16(1)	16(1)	15(1)
Study	13(1)	15(2) <sup>b</sup>	17(2)	17(2)	15(3)
P-value	0.69	0.27	0.53	0.47	0.62
Airway resistance (cm·H <sub>2</sub> O L <sup>-1</sup> ·s <sup>-1</sup> )					
Control	11(3)	20(3) <sup>b</sup>	23(6)	23(6)	13(4)
Study	10(3)	19(5) <sup>b</sup>	19(6)	19(7)	12(3)
P-value	0.19	0.37	0.06	0.07	0.18

Data are presented as mean (SD).  $P < 0.05$  in all groups.

PEEP = positive end-expiratory pressure.

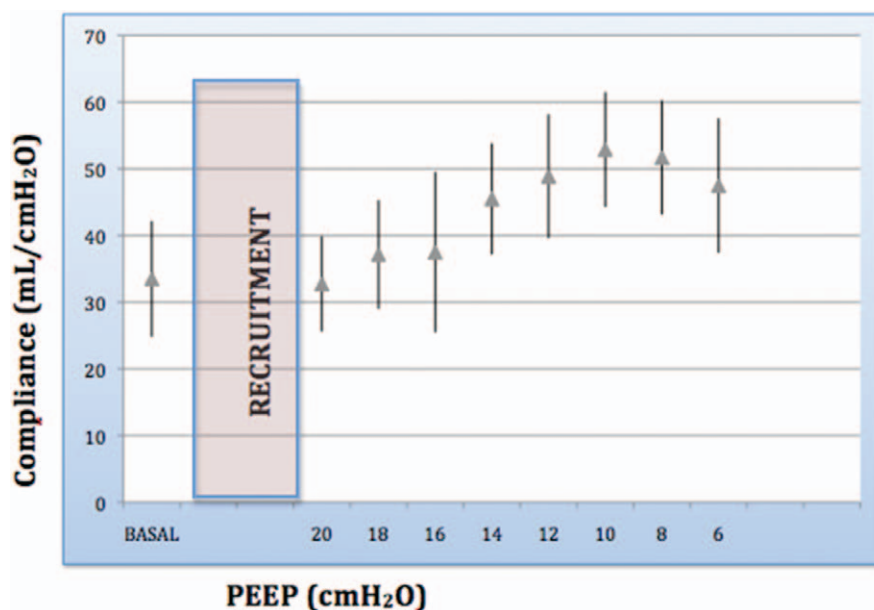
<sup>a</sup>Control versus study.

<sup>b</sup>Bilateral versus one-lung ventilation, prerecruitment maneuver.

<sup>c</sup>One-lung ventilation prerecruitment maneuver versus 20 minutes after peep during one-lung ventilation, and end one-lung ventilation,  $P$  value for control versus study difference.

open, while an inadequate PEEP level could not prevent alveolar recollapse after an alveolar recruitment maneuver in thoracic surgeries.

Our results are in agreement with other studies, showing that PEEP improves oxygenation during one-lung ventilation. However, the effects of different PEEP levels on



**Figure 3.** Dynamic compliance versus PEEP in the study group during the PEEP decrement trial. Data are presented as mean (SD).

oxygenation during one-lung ventilation have been controversial, because heterogeneity in lung pathology produces different responses to PEEP. Michelet et al.<sup>13</sup> found that 5 and 10 cm-H<sub>2</sub>O of PEEP improved oxygenation to the same degree, but 15 cm-H<sub>2</sub>O worsened oxygenation because over distension can increase shunt by diverting pulmonary blood flow to nonaerated areas. Several studies showed that 4 to 5 cm-H<sub>2</sub>O of PEEP during one-lung ventilation improved oxygenation, but increasing PEEP level to 8 to 10 cm-H<sub>2</sub>O did not improve oxygenation and was sometimes counterproductive.<sup>16,17</sup> Leong et al.<sup>18</sup> compared PEEP levels 0, 5, 8, and 10 cm-H<sub>2</sub>O during one-lung ventilation and found no differences in oxygenation.

Based on these results, several authors have promoted the use of 5 cm-H<sub>2</sub>O during one-lung ventilation for all patients.<sup>11,21,35</sup> However, some studies suggest that it is unreasonable to apply a standardized PEEP level for all patients during one-lung ventilation and that PEEP levels should be individualized. Valenza et al.<sup>19</sup> showed that PEEP was more effective in nonobstructive patients (high forced expiratory volume in 1 second) with lower risk of auto-PEEP than in patients with low high forced expiratory volume in 1 second. Slinger and Scott<sup>36</sup> also showed that PEEP effectiveness regarding oxygenation and lung mechanics depends on the interaction between PEEP and auto-PEEP, which in turn depends on patient mechanical characteristics. In another study, Slinger et al.<sup>12</sup> showed that PEEP effectively prevented atelectasis, but that the applied PEEP level should be individualized based on the static compliance curve.

The physiological and clinical effects of a particular level of PEEP are different when PEEP is used isolated or in combination with an alveolar recruitment maneuver.<sup>37</sup> Therefore, it is difficult to compare the above studies with the ones by using the concept of lung recruitment.

Alveolar recruitment maneuver strategies are not routinely done by anesthesiologists during one-lung ventilation and are usually conducted only when hypoxemia

appears.<sup>11,35,38</sup> However, previous studies have shown that an alveolar recruitment maneuver during one-lung ventilation improves oxygenation, ventilation efficiency, and lung mechanics due to reopening of atelectatic areas.<sup>22–26</sup> Each of these studies fixed PEEP levels between 5 and 10 cm-H<sub>2</sub>O without determining individual optimized PEEP settings. Therefore, the difference between using a standard PEEP level versus an individualized level after an alveolar recruitment maneuver in one-lung ventilation has not been elucidated.

Optimal PEEP is defined as the post-alveolar recruitment maneuver PEEP level that prevents alveolar collapse while minimizing overdistension. Optimal PEEP encourages maximal arterial oxygen tension and compliance and minimal dead-space<sup>29</sup> in restrictive,<sup>27</sup> healthy,<sup>37</sup> and obstructive<sup>12</sup> lungs. Our study showed that the improved oxygenation after an alveolar recruitment maneuver was only maintained at the end of one-lung ventilation in the group with an individualized PEEP level. These results suggest that an optimal PEEP level keeps the lung open, while 5 cm-H<sub>2</sub>O of PEEP level may not prevent alveolar recollapse or derecruitment. Despite the differences of PEEP with and without an alveolar recruitment maneuver, our results are not comparable with previous studies due to methodological differences. First, we recruited both groups; to our knowledge, this is the first study comparing the effects of individualized PEEP and standardized PEEP after applying an alveolar recruitment maneuver in both groups. Second, we performed the alveolar recruitment maneuver during one-lung ventilation. Cinnella et al.<sup>24</sup> and Tusman et al.<sup>25</sup> recruited during one-lung ventilation, but they established a standardized PEEP level in all patients and did not evaluate oxygenation at the end of one-lung ventilation.

Our hypothesis was reinforced by the lung mechanics results. In the study group, static compliance improved after the alveolar recruitment maneuver, and the improvement was maintained during the whole procedure with one-lung ventilation. In contrast, in the control group,

the postalveolar recruitment maneuver static compliance improvement was lost, presumably due to alveolar re-collapse. These results are compatible with those obtained by Unzueta et al.<sup>26</sup> and Park et al.,<sup>23</sup> who found no differences in static compliance between groups with and without an alveolar recruitment maneuver when a fixed PEEP was applied.

Previous studies<sup>22-26</sup> showed that an alveolar recruitment maneuver decreases the dead-space effect produced by atelectasis and improves ventilation efficiency as demonstrated by reduced alveolar dead-space volume/alveolar tidal volume in cardi thoracic surgery. We hypothesized that an optimal PEEP level might more effectively maintain the benefits of an alveolar recruitment maneuver in terms of ventilation efficiency, compared with by using a standardized PEEP level; however, our results did not confirm this. We believe that the lack of difference in dead space observed between groups depended on the amount of lung collapse. Because both groups were recruited, it is reasonable to think that the control group kept some recruitment effect by 5 cm-H<sub>2</sub>O of PEEP and that such an effect minimized the difference in dead space. Alveolar dead-space volume/alveolar tidal volume increased <5% in our study while Unzueta et al.<sup>26</sup> showed an increase >35% because an alveolar recruitment maneuver was not performed in their control patients. Increased levels of atelectasis in patients make the changes produced by an alveolar recruitment maneuver more evident.

Despite a lack of statistical differences in pH, PaCO<sub>2</sub> was significantly higher in the study group than in the control group. Based on the results of previous studies,<sup>39</sup> this may have contributed to a decreased shunt and improved oxygenation in the study group through an improvement in hypoxic pulmonary vasoconstriction. This limitation should be considered in future studies.

In concordance with previous studies, we found no differences in cardiac index between groups with different levels of PEEP.<sup>40</sup> No clinically relevant changes to cardiac index occurred during the alveolar recruitment maneuver.

Our study has some limitations. The main limitation of the study is that our discussion is based on the effects of the alveolar recruitment maneuver and PEEP on atelectasis without providing evidence from lung images or shunt measurements. Previous studies showed the effect of an alveolar recruitment maneuver on shunt and/or atelectasis by using a computed tomography scan and magnetic resonance images.<sup>27,41</sup> We determined the effect of lung recruitment by using classical indirect measurements such as Pao<sub>2</sub>, static compliance and alveolar dead space. The second limitation is that the use of 100% Fio<sub>2</sub> may have contributed to an increase in the amount of reabsorption atelectasis, thereby reducing Pao<sub>2</sub> in the control group. In this way, the use of lower levels of Fio<sub>2</sub> may have varied the differences in oxygenation observed between groups. However, the use of 100% Fio<sub>2</sub> is the first rescue therapy when hypoxemia appears. In this case, the use of an individualized level of PEEP would prevent reabsorption atelectasis more than a standardized level of PEEP.

In conclusion, the present results showed that during one-lung ventilation, the effects of an alveolar recruitment maneuver on lung function is better preserved with an

individualized level of PEEP based on a PEEP decrement trial compared with that of simple arbitrary PEEP levels of 5 cm-H<sub>2</sub>O. ■■

## DISCLOSURES

**Name:** Carlos Ferrando, MD, PhD.

**Contribution:** This author helped with study design, acquisition and analysis of data, interpretation of data, and writing the article.

**Attestation:** Dr. Ferrando approved the final manuscript, attests to the integrity of the original data and the analysis reported in this manuscript, and is the archival author.

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**Contribution:** This author helped with study design.

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**Contribution:** This author helped with interpretation of data, drafting, and revising the manuscript.

**Attestation:** Dr. Tusman approved the final manuscript.

**Name:** Francisco Javier Belda, MD, PhD.

**Contribution:** This author helped with interpretation of data, drafting, and revising the article.

**Attestation:** Dr. Belda approved the final manuscript and attests to the integrity of the original data and the analysis reported.

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## REFERENCES

1. Duggan M, Kavanagh BP. Pulmonary atelectasis: a pathogenic perioperative entity. *Anesthesiology* 2005;102:838-54
2. Licker M, de Perrot M, Höhn L, Tschopp JM, Robert J, Frey JG, Schweizer A, Spiliopoulos A. Perioperative mortality and major cardio-pulmonary complications after lung surgery for non-small cell carcinoma. *Eur J Cardiothorac Surg* 1999;15:314-9
3. van der Werff YD, van der Houwen HK, Heijmans PJ, Duurkens VA, Leusink HA, van Heesewijk HP, de Boer A. Postpneumonectomy pulmonary edema. A retrospective analysis of incidence and possible risk factors. *Chest* 1997;111:1278-84
4. Licker M, de Perrot M, Spiliopoulos A, Robert J, Diaper J, Chevalley C, Tschopp JM. Risk factors for acute lung injury after thoracic surgery for lung cancer. *Anesth Analg* 2003;97:1558-65
5. Slinger PD. Acute lung injury after pulmonary resection: more pieces of the puzzle. *Anesth Analg* 2003;97:1555-7
6. Choi G, Wolthuis EK, Bresser P, Levi M, van der Poll T, Dzoljic M, Vroom MB, Schultz MJ. Mechanical ventilation with lower tidal volumes and positive end-expiratory pressure prevents alveolar coagulation in patients without lung injury. *Anesthesiology* 2006;105:689-95
7. Cohen E, Eisenkraft JB. Positive end-expiratory pressure during one-lung ventilation improves oxygenation in patients with low arterial oxygen tensions. *J Cardiothorac Vasc Anesth* 1996;10:578-82
8. Eisenkraft J, Cohen E, Neustein S. Anesthesia for thoracic surgery. In: Barash P, Cullen B, Stoelting R, eds. *Clinical Anesthesia*, 3rd ed. Philadelphia, PA: Lippincott-Raven, 1997;779-84
9. Fujiwara M, Abe K, Mashimo T. The effect of positive end-expiratory pressure and continuous positive airway pressure on the



- oxygenation and shunt fraction during one-lung ventilation with propofol anesthesia. *J Clin Anesth* 2001;13:473–7
10. Loshier J. Evidence-based management of one-lung ventilation. *Anesthesiology Clin* 2008;26:241–72
11. Grichnik KP, Shaw A. Update on one-lung ventilation: the use of continuous positive airway pressure ventilation and positive end-expiratory pressure ventilation—clinical application. *Curr Opin Anesthesiol* 2009;22:23–30
12. Slinger PD, Kruger M, McRae K, Winton T. Relation of the static compliance curve and positive end-expiratory pressure to oxygenation during one-lung ventilation. *Anesthesiology* 2001;95:1096–102
13. Michelet P, Roch A, Brousse D, D'Journo XB, Bregeon F, Lambert D, Perrin G, Papazian L, Thomas P, Carpentier JP, Auffray JP. Effects of PEEP on oxygenation and respiratory mechanics during one-lung ventilation. *Br J Anesth* 2005;95:267–73
14. Hoftman N, Canales C, Leduc M, Mahajan A. Positive end expiratory pressure during one-lung ventilation: selecting ideal patients and ventilator settings with the aim of improving arterial oxygenation. *Ann Card Anesth* 2011;14:183–7
15. Inomata S, Nishikawa T, Saito S, Kihara S. "Best" PEEP during one-lung ventilation. *Br J Anaesth* 1997;78:754–6
16. Abe K, Shimizu T, Takashina M, Shiozaki H, Yoshiya I. The effects of propofol, isoflurane, and sevoflurane on oxygenation and shunt fraction during one-lung ventilation. *Anesth Analg* 1998;87:1164–9
17. Sentürk NM, Dilek A, Camci E, Sentürk E, Orhan M, Tuğrul M, Pembeci K. Effects of positive end-expiratory pressure on ventilatory and oxygenation parameters during pressure-controlled one-lung ventilation. *J Cardiothorac Vasc Anesth* 2005;19:71–5
18. Leong LM, Chatterjee S, Gao F. The effect of positive end expiratory pressure on the respiratory profile during one-lung ventilation for thoracotomy. *Anesthesia* 2007;62:23–6
19. Valenza F, Ronzoni G, Perrone L, Valsecchi M, Sibilla S, Nosotti M, Santambrogio L, Cesana BM, Gattinoni L. Positive end-expiratory pressure applied to the dependent lung during one-lung ventilation improves oxygenation and respiratory mechanics in patients with high FEV1. *Eur J Anaesthesiol* 2004;21:938–43
20. Della Rocca G, Coccia C. Ventilatory management of one-lung ventilation. *Minerva Anesthesiol* 2011;77:534–6
21. Karzai W, Schwarzkopf K. Hypoxemia during one-lung ventilation: prediction, prevention, and treatment. *Anesthesiology* 2009;110:1402–11
22. Tusman G, Böhm SH, Sipmann FS, Maisch S. Lung recruitment improves the efficiency of ventilation and gas exchange during one-lung ventilation anesthesia. *Anesth Analg* 2004;98:1604–9, table of contents
23. Park SH, Jeon YT, Hwang JW, Do SH, Kim JH, Park HP. A preemptive alveolar recruitment strategy before one-lung ventilation improves arterial oxygenation in patients undergoing thoracic surgery: a prospective randomised study. *Eur J Anesthesiol* 2011;28:298–302
24. Cinnella G, Grasso S, Natale C, Solitto F, Cacciapaglia M, Angiolillo M, Pavone G, Mirabella L, Dambrosio M. Physiological effects of a lung-recruiting strategy applied during one-lung ventilation. *Acta Anaesthesiol Scand* 2008;52:766–75
25. Tusman G, Böhm SH, Melkun F, Staltari D, Quinzio C, Nador C, Turchetto E. Alveolar recruitment strategy increases arterial oxygenation during one-lung ventilation. *Ann Thorac Surg* 2002;73:1204–9
26. Unzueta C, Tusman G, Suarez-Sipmann F, Böhm S, Moral V. Alveolar recruitment improves ventilation during thoracic surgery: a randomized controlled trial. *Br J Anaesth* 2012;108:517–24
27. Suarez-Sipmann F, Böhm SH, Tusman G, Pesch T, Thamm O, Reissmann H, Reske A, Magnusson A, Hedenstierna G. Use of dynamic compliance for open lung positive end-expiratory pressure titration in an experimental study. *Crit Care Med* 2007;35:214–21
28. Tusman G, Suarez-Sipmann F, Böhm SH, Pech T, Reissmann H, Meschino G, Scandurra A, Hedenstierna G. Monitoring dead space during recruitment and PEEP titration in an experimental model. *Intensive Care Med* 2006;32:1863–71
29. Maisch S, Reissmann H, Fuellekrug B, Weismann D, Rutkowski T, Tusman G, Böhm SH. Compliance and dead space fraction indicate an optimal level of positive end-expiratory pressure after recruitment in anesthetized patients. *Anesth Analg* 2008;106:175–81, table of contents
30. Brinkman R, Amadeo RJ, Funk DJ, Girling LG, Grocott HP, Mutch WA. Cerebral oxygen desaturation during one-lung ventilation: correlation with hemodynamic variables. *Can J Anaesth* 2013;60:660–6
31. Haas S, Eichhorn V, Hasbach T, Trepte C, Kutup A, Goetz AE, Reuter DA. Goal-directed fluid therapy using stroke volume variation does not result in pulmonary fluid overload in thoracic surgery requiring one-lung ventilation. *Crit Care Res Pract* 2012;2012:687018
32. Enghoff H. Volumen inefficax. Bemerkungen zur Frage des schädlichen Raumes. *Uppsala Läkareforen Forhandl* 1938;44:191–218
33. Bardoczky GI, d'Hollander AA, Cappello M, Yernault JC. Interrupted expiratory flow on automatically constructed flow-volume curves may determine the presence of intrinsic positive end-expiratory pressure during one-lung ventilation. *Anesth Analg* 1998;86:880–4
34. Brunner E, Munzel U. The nonparametric Behrens-Fisher problem: asymptotic theory and a small-sample approximation. *Biometrical J* 2000;42:17–25
35. Sentürk M. New concepts of the management of one-lung ventilation. *Curr Opin Anesthesiol* 2006;19:1–4
36. Slinger P, Scott WA. Arterial oxygenation during one-lung ventilation. A comparison of enflurane and isoflurane. *Anesthesiology* 1995;82:940–6
37. Tusman G, Böhm SH, Vazquez de Anda GF, do Campo JL, Lachmann B. 'Alveolar recruitment strategy' improves arterial oxygenation during general anaesthesia. *Br J Anaesth* 1999;82:8–13
38. Ren Y, Peng ZL, Xue QS, Yu BW. The effect of timing of application of positive end-expiratory pressure on oxygenation during one-lung ventilation. *Anesth Intensive Care* 2008;36:544–8
39. Toth I, Leiner T, Mikor A, Szakmany T, Bogar L, Molnar Z. Hemodynamic and respiratory changes during lung recruitment and descending optimal positive end-expiratory pressure titration in patients with acute respiratory distress syndrome. *Crit Care Med* 2007;35:787–93
40. Nilsson MC, Fredén F, Larsson A, Wiklund P, Bergquist M, Hambraeus-Jonzon K. Hypercapnic acidosis transiently weakens hypoxic pulmonary vasoconstriction without affecting endogenous pulmonary nitric oxide production. *Intensive Care Med* 2012;38:509–17
41. Rothen HU, Neumann P, Berglund JE, Valtysson J, Magnusson A, Hedenstierna G. Dynamics of re-expansion of atelectasis during general anaesthesia. *Br J Anaesth* 1999;82:551–6